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| 09/945,145 | 08/31/2001 | Robert S. Matson | 1984-045 | 3127 |

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| EXAMINER |
|---|
| CHAKRABARTI, ARUN K |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

DATE MAILED: 01/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/945,145 | Matson |
| **Examiner** | **Art Unit** |
| Arun Chakrabarti | 1655 |

-- **The MAILING DATE of this communication appears on the cover sheet with the correspondence address** --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1) ☒ Responsive to communication(s) filed on Aug 31, 2001 .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

**Disposition of Claims**

4) ☒ Claim(s) 1-72 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-72 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

**Application Papers**

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 2

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

## DETAILED ACTION

### *Claim Objections*

1. Claim 33 is objected to because of the following informalities: Claim 33 is duplicate of claim 32. Applicant is hereby suggested to cancel claim 33. Appropriate correction is required.

### *Claim Rejections - 35 USC § 112*

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention..

Claim 21 recites the limitation "said target nucleic acid" in line 2. There is insufficient antecedent basis for this limitation in the claim.

### *Claim Rejections - 35 USC § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1, 3, 7, 9, 11-14, 17-18, 22-28, 53, 55-58, 62 and 66-71 are rejected under 35 U.S.C. 102 (b) as being anticipated by Jahn et al. (Proceedings of the National Academy of Sciences, USA, (1984), Vol. 81, pages 1684-1687).

Jahn et al teach a method for detecting one or more target biopolymer analyte in a sample (Abstract), comprising:

a) preparing a microarray of the sample by dispensing aliquots of the sample at discrete sites onto a substrate and immobilizing the analytes on the substrate, wherein each of the aliquots contains the same amount of the target analytes (Abstract, and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection);

b) contacting the microarray with a plurality of labeled probes specific for each of the target analytes under conditions that allow formation of a complex between each of the target analytes and the labeled probes specific for the target analyte (Abstract, and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection); and

c) detecting the complexes as a measurement of the presence or the amount of the target analytes (Abstract, and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection and Figures 1-5).

Jahn et al teach a method, wherein the aliquots comprise picomole amounts of the target biopolymer selected from ligands or receptors polypeptides (Abstract).

Jahn et al teach a method, wherein the target biopolymer is a receptor and the probe biopolymer is a ligand for the receptor (Abstract, and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein the target biopolymer is an antigen and the probe biopolymer is an antibody specific for the antigen (Abstract, and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein the probe is labeled with a reporter radioactive-labeled biomolecule (Abstract and Materials and Method Section, Page 1684, Materials Subsection).

Jahn et al teach a method, wherein the substrate is made of nitrocellulose (Abstract and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein the target biopolymer is immobilized on the substrate by direct adsorption (Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein the support is in the form of sheets (Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein in step (b), the microarray is contacted with a plurality of probes (Abstract and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein each aliquot is contacted with a different probe (Abstract and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein the probes are labeled with identical reporter groups (Abstract and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein the probes are labeled with reporters that are distinguishable from one another (Abstract and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein in step (b), each of the aliquots is contacted with a plurality of probes (Abstract and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

Jahn et al teach a method, wherein the aliquots are deposited onto the substrate at about 3 sites per square millimeter of the substrate surface area . This calculation has been made from the total area of grid of squares (1.8 X 1.8 cm) and area of each spot having diameter 1.2-1.5 cm (Abstract and Materials and Method Section, Page 1684, Column 2, Standard Procedure for the Dot-Immunoblotting Assay Subsection).

6. Claims 1, 7, 8, 10, 13-14, 17-18, 21-24, 26, 28, 30, 37-40, 44-47, 49, 53, 55-57, 62, 66-68, and 70 are rejected under 35 U.S.C. 102 (b) as being anticipated by Shuber et al. (Human Molecular Genetics (1997), Vol. 6 (3), pages 337-347).

Shuber et al teach a method for detecting one or more target biopolymer analyte in a sample (Abstract), comprising:

a) preparing a microarray of the sample by dispensing aliquots of the sample at discrete sites onto a substrate and immobilizing the analytes on the substrate, wherein each of the aliquots contains the same amount of the target analytes (Abstract, and Results Section, Mutation Detection Subsection and Figures 1 and 3);

b) contacting the microarray with a plurality of labeled probes specific for each of the target analytes under conditions that allow formation of a complex between each of the target analytes and the labeled probes specific for the target analyte (Abstract, and Results Section, Mutation Detection Subsection and Figures 1 and 3); and

c) detecting the complexes as a measurement of the presence or the amount of the target analytes (Abstract, and Results Section, Mutation Detection Subsection and Figures 1 and 3).

Shuber et al teach a method, wherein the target biopolymer or the probe biopolymer is selected from polynucleotides and amplified DNA (Abstract and Results Section, Mutation Detection Subsection and Figures 1 and 3).

Shuber et al teach a method, wherein the target biopolymer is a polynucleotide and the probe biopolymer is a polynucleotide that is complementary to the target polynucleotide (Abstract).

Shuber et al teach a method, wherein the probe is labeled with a reporter radioactive-labeled biomolecule (Abstract and Figures 3 and 6 and MATERIALS AND METHODS Section, Probe labeling Subsection).

Shuber et al teach a method, wherein the substrate is made of nylon (Biotrans) membranes (Abstract and Figures 1, 3, and 6 and MATERIALS AND METHODS Section, Dot Blot Subsection).

Shuber et al inherently teach a method, wherein the target biopolymer is immobilized on the substrate by direct adsorption (Figures 1, 3, and 6 and MATERIALS AND METHODS Section, Dot Blot Subsection).

Shuber et al teach a method, further comprising co-dispensing an internal standard with the sample to determine the concentration of the target nucleic acid in the aliquots (MATERIALS AND METHODS Section, Hybridization/ASO pooling Subsection).

Shuber et al teach a method, wherein in step (b), the microarray is contacted with a plurality of different probes (Abstract and Figures 1, 3, and 6 and MATERIALS AND METHODS Section, Dot Blot Subsection and Hybridization/ASO pooling Subsection).

Shuber et al teach a method, wherein the probes are labeled with identical reporter groups (Abstract and Figures 1, 3, and 6 and MATERIALS AND METHODS Section, Dot Blot Subsection and Probe labeling Subsection).

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-19, 21-42, 44-64, and 66-72 are rejected under 35 U.S.C. 103 (a) over Shuber et al. (Human Molecular Genetics (1997), Vol. 6 (3), pages 337-347) in view of Balch et al. (U.S. Patent 6,312,960 B1) (November 6, 2001).

Shuber et al teach method of claims 1, 7, 8, 10, 13-14, 17-18, 21-24, 26, 28, 30, 37-40, 44-47, 49, 53, 55-57, 62, 66-68, and 70 as described above.

Shuber et al. do not teach the aliquots comprising picomole, femtomole, attomole or zeptomole amounts of the target biopolymer.

However, it is *prima facie* obvious that selection of a particular concentration of the target biopolymer represents routine optimization with regard to the complementarity, strength and titer of the probe biopolymer to be hybridized to the target biopolymer, which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of a particular concentration of the target biopolymer was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Shuber et al do not teach the method, wherein the preparation of microarray further comprises dispensing the sample aliquots on the substrate by a capillary quill contact printing method and jet printing method.

Balch et al. teach the method, wherein the preparation of microarray further comprises dispensing the sample aliquots on the substrate by a capillary quill contact printing method and jet printing method (Figures 3 and 4a and abstract).

Shuber et al do not teach the method, wherein the polypeptide is selected from the group consisting of antibodies, ligands, and receptors.

Balch et al. teach the method, wherein the polypeptide is selected from the group consisting of antibodies, ligands, and receptors (Figure 17).

Shuber et al do not teach the method, wherein the target biopolymer is an antigen or receptor and the probe biopolymer is an antibody specific for the antigen or a ligand for the receptor respectively.

Balch et al. teach the method, wherein the target biopolymer is an antigen or receptor and the probe biopolymer is an antibody specific for the antigen or a ligand for the receptor respectively (Figure 17).

Shuber et al do not teach the method, wherein the crosslinked polymers are selected from polypropylene, polyethylene or polystyrene.

Balch et al. teach the method, wherein the crosslinked polymers are selected from plastics inherently made from polypropylene, polyethylene or polystyrene (Column 16, lines 42-53).

Shuber et al do not teach the method, wherein the surface-modified materials are modified with functional groups selected from amino, thiol, hydroxyl or carboxyl to contain hydrophobic and/or hydrophilic regions prior to dispensing steps.

Balch et al. teach the method, wherein the surface-modified materials are modified with functional groups selected from amino, thiol, hydroxyl or carboxyl to contain hydrophobic and/or hydrophilic regions prior to dispensing steps (Column 21, line 38 to Column 22, line 8).

Shuber et al do not teach the method, wherein the probes are labeled with reporters that are distinguishable from one another.

Balch et al. teach the method, wherein the probes are labeled with reporters that are distinguishable from one another (Column 25, line 19 to Column 27, line 6).

Shuber et al do not teach the method, wherein the aliquots are deposited onto a multiple well microplate substrate at between 1 to 1536 sites per well of the microplate.

Balch et al. teach the method, wherein the aliquots are deposited onto a multiple well microplate substrate at between 1 to 1536 sites per well of the microplate (Column 14, line 2 to Column 16, line 12 and Figure 14).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time

the invention was made to combine and substitute the methods for fabricating an array for use in mutiplexed biochemical analysis of Balch et al. in the method of high throughput parallel analysis of Shuber et al. since Balch et al. state, "The instant invention provides for both a multiplexed environment to rapidly determine optimal assay parameters, as well as a fast, cost-effective, and accurate system for the quantitative analysis of target analytes, thereby circumventing the limitations of single determination assays (Column 4, lines 5-9)." Balch et al further provide motivation as Balch et al. state, "Recent innovative adaptations of proximal charge-coupled device (CCD) technology has made it feasible to quantitatively detect and image molecular probe arrays incorporated into the bottom of microplate wells. This creates a high throughput platform of exceptional utility, capable of addressing several applications with very complex analysis parameters (Column 4, lines 25-31)". An ordinary practitioner would have been motivated to combine and substitute the methods for fabricating an array for use in mutiplexed biochemical analysis of Balch et al. in the method of hugh throughput parallel analysis of Shuber et al. in order to achieve the express advantage, as noted by Balch et al, of the assays of the invention, which provides for both a multiplexed environment to rapidly determine optimal assay parameters, as well as a fast, cost-effective, and accurate system for the quantitative analysis of target analytes, thereby circumventing the limitations of single determination assays and also the feasibility of quantitatively detecting and imaging molecular probe arrays incorporated into the bottom of microplate wells, which creates a high throughput platform of exceptional utility, capable of addressing several applications with very complex analysis parameters.

9. Claims 1-72 are rejected under 35 U.S.C. 103 (a) over Shuber et al. (Human Molecular Genetics (1997), Vol. 6 (3), pages 337-347) in view of Balch et al. (U.S. Patent 6,312,960 B1) (November 6, 2001) further in view of Sirvio et al. (U.S. Patent 5,532,311) (July 2, 1996).

Shuber et al. in view of Balch et al teach the method of claims 1-19, 21-42, 44-64, and 66-72 as described above.

Shuber et al. in view of Balch et al do not teach the method, wherein the substrate is wetted with an organic modifier selected from dextran sulfate or polyacrylic acid.

Sirvio et al. teach the method, wherein the substrate is wetted with an organic modifier selected from dextran sulfate or polyacrylic acid (Column 2, lines 45-64).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the process for modifying substrates of Sirvio et al. in the method of high throughput parallel analysis of Shuber et al in view of Balch et al, since Sirvio et al. state, "The invention provides a simple and effective means for modifying the surface of an article, e.g., to render that surface biocompatible. Surprisingly, the process is effective despite the fact that the priming operation is conducted in the absence of crosslinking agents (Column 2, lines 21-25)". An ordinary practitioner would have been motivated to combine and substitute the process for modifying substrates of Sirvio et al. in the method of high throughput parallel analysis of Shuber et al in view of Balch et al, in order to achieve the express advantage, as noted by Sirvio et al, of the invention, which provides a simple and effective means for modifying the surface of an article, e.g., to render that surface biocompatible and which is

surprisingly effective despite the fact that the priming operation is conducted in the absence of crosslinking agents.

***Conclusion***

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

**Arun Chakrabarti**
**Patent Examiner**
**Art Unit 1634,**

**January 14, 2003**

W. Gary Jones
Supervisory Patent Examiner
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